CARCINOMA OF THE NERVOUS SYSTEM, WITH THE REPORT OF ELEVEN CASES.*

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We have had the opportunity of studying eleven cases of carcinoma implicating the nervous system, eight of these were with necropsy. From a study of these cases and of others in the literature we have made the following classification:

First—Cases in which metastasis to the central nervous system occurs from a primary lesion elsewhere in the body.

Second—Those in which the alterations in the substance of the spinal cord and brain are not distinctly carcinomatous, but are such as may be caused by pressure, etc.

Third—Those in which the peripheral nerves are diseased either with or without involvement of the brain and cord.

Fourth—Those in which no macroscopic lesions are found, and possibly in some, no microscopic lesions, and the symptoms are supposedly toxic.

Metastasis in the central nervous system secondary to carcinoma elsewhere in the body may assume many forms. It may occur as a multiple carcinomatosis, which may or may not be a part of a general carcinomatous process elsewhere. There may be only a few cancer nodules within the central nervous system, or the process may involve the brain or cord and the meninges extensively, or the meninges alone. The meningeal infiltration may be either diffuse, as carcinomatous meningitis, like the sarcomatous meningitis, or may be in the form of multiple small tumors.

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Metastasis may occur anywhere in the brain. It is probable that cancer nodules occasionally are overlooked, either because of their resemblance to the surrounding brain tissue, or because of their minute size.

Metastasis to the substance of the spinal cord is extremely rare and is nearly always from the periphery of the cord. Metastasis in the vertebræ is more common.

In the second classification, in which alterations in the spinal cord or brain occur, which are not carcinomatous, the changes may be in the form of a diffuse sclerosis, or an acute inflammatory process. Occasionally in association with degenerative changes in the cord, there may be disease of the spinal roots and peripheral nerves.

In the third classification, viz., cases in which the peripheral nerves are diseased either with or without involvement of the brain and cord, the alterations in the peripheral nerves and muscles may be mild or severe. Raymond[1] has recently recorded a case in which the symptoms of multiple neuritis were present, but there was no cancerous invasion of the nerve trunks. The intramuscular nerve ramifications were diseased, and innumerable cancerous masses were found in the muscles; the condition was an acute miliary carcinomatosis, especially of the muscles.

In the fourth classification, in which the symptoms seem to be of toxic origin, may be included all those cases in which no gross pathological changes are found. The microscopic examination, however, may show alterations in the nerve cells in different parts of the brain and cord, sometimes a marked congestion of the blood vessels and degenerative changes in some of the cranial nerves. As toxic conditions, may be included the following: Hemiplegia, with or without aphasia, aphasia alone, monoplegia, convulsions, either general or Jacksonian in type; cranial nerve paralysis and bulbar phenomena. The psychoses which sometimes complicate carcinoma may also be placed here, although some authors believe that psychoses do not occur unless there be an intracranial metastasis.

It is noteworthy that in the majority of instances the symptoms are not so pronounced as might be expected from the pathological findings. This is either because many of the lesions produce no alteration of the surrounding tissue, or else the lesions, though apparently intense, are not sufficiently so to produce symptoms.

It will be impossible to consider in this paper the large amount of literature on the subject of carcinoma, and only the more important contributions will be referred to. It will be our purpose to dilate upon the classifications made, using such literature as is necessary and drawing our conclusions also from the cases we here record. It must of course be understood that the classification adopted is only relative, and that one case may have symptoms belonging to each division made.

Metastasis to the osseous and connective tissue coverings of the spinal cord occurs most often in sarcoma, and next in frequency in carcinoma. Schlesinger[2] in his monograph on tumors of the spinal cord and of the vertebræ, published in 1898, states that metastasis occurred to these coverings in 2.4% of the cases of carcinoma elsewhere in the body and in 8.8% of sarcoma elsewhere. His observations were drawn from 13,300 necropsies of all kinds. In another series of necropsy records of 35,000 cases carcinoma metastasis to the brain occurred as follows: cerebrum, 16; cerebellum, 8; medulla oblongata, 5; bones of the skull, 41; dura, 17; pia, 2; in all, 89 times. The conclusion can be drawn that metastasis of carcinoma to the nervous system occurs in the following order of frequency; vertebræ, bones of the skull, brain, and very rarely into the spinal cord.

In 1898 Buchholz[3] collected 66 cases of cancer of the brain, exclusive of tumors of the hypophysis and of the bones of the skull. Of these 41 were said to be secondary, 5 primary, and the remainder were more or less doubtful. Two of the primary growths originated in the epithelium of the fourth ventricle (Wunschheim[4]) or the aqueduct of Sylvius (Coats[5]). The three other cases are regarded by Buchholz as questionable. Besides these cases which are quoted by Buchholz, Ziegler is said to have recorded a papillomatous cancerous growth of the choroid plexus and Cornil and Ranvier a similar growth of the third ventricle. Another similar case of Spaet is often quoted in the literature, but we have been unable to obtain the original paper.

Metastasis occurs more often from a primary growth situated in the mammary gland, lung or pleura, in the order mentioned.

It also occurs secondary to cancer of the stomach, pancreas, ovaries, testicles, uterus and rectum.

Metastasis to the nervous system may occur:

1. Into the vertebræ.
2. Into the bones of the skull.
3. Into the substance of the brain, cord and meninges.
4. Into the brain alone.
5. Into the substance of the brain and cord.
6. Into the meninges alone.
7. Into the spinal cord alone.

Secondary carcinoma of the brain is often multiple, and may be part of a general carcinomatosis elsewhere, as in Case IV. of Gallavardin and Varay[6] in which from 150 to 250 cancer nodules were found in the brain, and others were in the cord. Metastasis may involve almost any portion of the brain, but the central convolutions seem to be frequently involved as in the cases of Blum[7] and Gallavardin and Varay[6] (Case I.).

Next in frequency are perhaps the cerebellar lobes as in the cases of Saenger[8] and Gallavardin and Varay[6] (Case II.). The temporal lobes are also sometimes involved, as in the case of Kufs[9] in which there was also a cancer of the pons and in Case II. of Gallavardin and Varay[6]. In Case I. of our series, a secondary growth of the hypophysis was found, as in the recent case of Götzel and Erdheim[10].

The cancer nodules may be as large as a hazel nut or even larger, or may be of microscopic size. When the nodules are small many may be overlooked unless a thorough microscopic examination is made. In multiple carcinomatosis of the nervous system, as in the cases of Buchholz[3], Siefert[11] and others, the cancer nodules are situated chiefly near the cortex, although they may be numerous in the white matter also. Sometimes numerous small cancer nodules may become confluent forming one large mass. The inner portion of the brain may become involved because of the extension of the process by means of the arteries.

Except in the instances in which there is a general carcinomatous process, the spinal cord is rarely involved. Metastasis to the spinal cord is so extremely rare that we have been unable to find a single instance of uncomplicated cancerous metastasis to the substance of the spinal cord, except perhaps in the case of Kolisko, which Schlesinger[2] (p. 82) quotes.

Metastasis into the spinal cord occurs occasionally in conjunction with vertebral carcinomatosis, as in the first case with necropsy recorded by Ballet and Laignel-Lavastine[12], in which a cancerous embolus of a dural artery caused a secondary growth. It is not infrequent to find a diffuse infiltration of cancer cells in the spinal cord in conjunction with meningeal carcinomatosis. Schlesinger also mentions a case of Ewald's in which there was an isolated cancer nodule in the cauda equina. A similar instance is recorded by Scanzoni[13]. In this case, however, there was in addition carcinoma of the vertebræ and multiple carcinomatosis of the brain and cord.

Secondary carcinoma may not only involve the substance of the brain and cord, but also the meninges. In an able paper Siefert[11], in 1903, called attention to this subject and recorded four such cases, besides reviewing the literature. In nearly all of these cases there is dissemination of cancer nodules throughout the brain, and rarely in the cord, invasion of the pia with rapid extension of the cancer cells within the pericerebral and perispinal spaces and though not constant, secondary infiltration of the meninges over the brain, spinal cord and spinal roots.

The extent of the meningeal infiltration varies of course, and depends upon the number and size of the cancerous tumors. Siefert believed that at least in those cases in which the tumors are peripheral and reach the pia, meningeal infiltration is possible. This, however, does not always occur, for cases are recorded in which meningeal infiltration was absent although the tumor mass invaded the cortex and pia.

The meningeal infiltration, according to Siefert, usually begins in the cerebral meninges and rarely in the spinal. Again, spinal infiltration may be entirely absent. The infiltration may be either in the form of a continuous mass or as a flat tumor, or may be in separate masses. The former is the more common. In general it may be said that carcinomatous meningitis resembles greatly sarcomatous meningitis, both in its pathological and clinical peculiarities. Among the authors who have recorded such cases, in addition to Siefert, are Lilienfeld and Bender[14], and Scanzoni[13].

Meningeal infiltration may be present alone, without involvement of the nervous tissues. Such are the cases of Saenger[15], in which there was a pial infiltration at the base or the brain and also in the lateral surface, and of Hellendall[16], in which there was a diffuse carcinomatous infiltration of the cerebral dura.

As is well known, vertebral carcinomatosis is a frequent form of cancerous involvement. We will not discuss this subject extensively, as we[17] have written before about vertebral carcinomatosis, and will only consider the unusual complications. As a rule the cancer cells invade the space between the bone and the dura mater, and exceptionally, the cancerous cells surround the entire dura and the spinal roots. Very exceptionally, the cancer cells penetrate into the dura and more rarely into the spinal cord itself. Such are the cases of Ballet and of Laignel-Lavastine[12]. Taylor and Waterman[18] recorded an exceptional case in which the cancer cells invaded the spinal membranes and were entirely within the dura. The infiltration surrounded the whole spinal cord and infiltrated both the anterior and posterior spinal roots, and in the postero-lateral portion invaded the spinal cord.

The rapid involvement of the spinal cord which is sometimes seen in the course of carcinomatosis has always excited great interest. An acute myelitis may occur without the slightest pressure, and is generally explained as a result of intoxication.

Although the primary growth may be a scirrhous cancer, metastatic tumors of the nervous system generally contain more cancer cells and less stroma. On account of growth of vascular connective tissue the tumor may appear papillomatous. The secondary cancer masses found in the ventricles can always be differentiated from the primary growths by the scarcity of connective tissue in the former (Kufs). This was well shown in the case of Kufs.

Within the cancer nodules hemorrhages and areas of softening are sometimes observed. The nervous structures around the cancer growth are only slightly altered, there being perhaps a little glia cell increase, as the nervous tissues are pushed aside and destroyed.

It has perhaps been insufficiently recognized that carcinoma of any organ of the body, but especially of the nervous system, may cause degenerative changes in the nerve cells of the brain and spinal cord at parts remote from the tumor. Whether this is the result of an auto-intoxication, or of a toxin of cancer, or of cachexia, or perhaps of all of these causes, is a difficult question to answer. We have found in our cases in which metastasis occurred either to the brain or to the vertebræ, disease of the nerve cells of different parts of the brain and cord. This subject will be further discussed under toxic changes.

It may be said that the clinical diagnosis of carcinoma of the nervous system is most difficult. The principal reason for this is the multiplicity of the lesions. Most varied diagnoses have been made in cases of carcinoma: brain tumor, hysteria, and syphilis being the most common. Whenever cancer occurs in any of the viscera, subsequent nervous symptoms should cause immediate suspicion of metastasis; but the diagnosis is often difficult because the primary lesion is not detected. Even the diagnosis of the vertebral carcinomatosis may offer difficulties, for as we have here pointed out in a previous communicaton[17], it is sometimes difficult to differentiate between multiple neuritis, spinal caries and vertebral carcinomata.

Alterations in the Nervous System Not Due to Metastasis.

The diffuse degenerations in the spinal cord which sometimes accompany cachexias are well known. Lubarsch[19], for instance, examined the spinal cords of nineteen cases of cancer of different regions and found alterations in eleven. These consisted mostly of a diffuse degeneration of the posterior and lateral columns, such as are found in anemias and other cachectic conditions. Sometimes the anterior columns may also be partially diseased. It is not uncommon to find accompanying these diffuse degenerations, disease of the spinal roots, especially the posterior, and also of the peripheral nerves.

Meyer[20] recorded an exceptional case in which the symptoms of primary disease of the pyramidal tracts appeared, at the same time as the symptoms of a primary cancer of the uterus.

The involvement of the spinal cord may be in the form of an acute myelitis. This may appear independently of any other involvement of the spinal cord, as in the case of Nonne, or may accompany vertebral carcinomata, independently of any compression of the cord.

Clinically the diagnosis of diffuse degeneration of the spinal cord occurring in carcinoma is not always made. This is sometimes because of mild spinal involvement, but mostly because of the preponderance of the other symptoms. It is still a question whether these lesions are the result of a toxin, or merely of a cachectic condition. The latter probably is the more potent cause.

Alterations in the Peripheral Nerves and Muscles.

The peripheral nerves may be involved in three ways. First, by direct contact with the cancer growth, as in a vertebral cancer, or as in Case I. of our series in which the oculomotor nerve was partially involved by the growth in the hypophysis. Second, there may be an acute neuritis due to the cancer toxin, or a chronic inflammation due to the cachexia. Third, the peripheral nerves may be normal, but, as in the case of Raymond[1], the finest intramuscular nerve endings may be implicated by innumerable cancerous masses in the muscles, a true carcinomatous neuromyositis.

The symptoms may come on acutely, as in the case of Francotte[22] (Case 2). In our Case III. the patient had alcoholic multiple neuritis, but in the course of a year most of the symptoms disappeared, although the reflexes remained lost. Later the symptoms of an esophageal cancer appeared, and coincident with this, the neuritic symptoms reappeared, and became gradually more acute. This case illustrates well the influence of cancer toxin on peripheral nerves. Alterations in the peripheral nerves and muscles without any symptoms are common, and are probably caused by the cachexia, as in our Case II. in which the peripheral nerves of one hand were degenerated, although there were no symptoms. Similar instances have been recorded by many authors, as Auché[23], Oppenheim and Siemerling[24], and others. Histologically the alterations are chiefly parenchymatous.

Besides a multiple neuritis, a neuritis of one or a number of cranial nerves or of a plexus, may occur. For instance, in our Case VII. several cranial nerves were paralyzed, while at necropsy, a degeneration of all of these nerves affected clinically was not found. Such alterations are undoubtedly toxic, and will be considered under that head. At times paralysis of a brachial plexus may occur, and this may be caused by the proximity of a cancer of the breast, the cancer poison being carried by the lymphatics.

Changes in the Nervous System Due to Carcinoma Toxin.

Some authors still dispute as to whether the rather bizarre nervous symptoms which may occur in the course of carcinoma are of toxic origin. Saenger, for instance, believes that definite organic changes cause the so-called toxic symptoms, while other authors believe that gastric intoxications are the cause. However, there is no doubt that different symptoms may appear in a case of carcinoma in which at necropsy no macroscopical lesions are found to explain them, but by microscopic examination diffuse changes may be discovered, which are not commensurate with the clinical symptoms.

Such a disease as carcinoma exerts a powerful influence upon the various functions of the body, the intensity of which probably depends upon the nature of the growth plus the inherent resistance of the nervous system to untoward influences. In no other manner can we explain the occasional involvement of the nervous system in carcinoma of other structures.

The nerve cells in carcinoma are particularly susceptible. Thus Sirleo[25] in two different cases of cancer of the abdominal walls examined the nervous system by the different modern staining methods, and was able to demonstrate by the Nissl method a degeneration of the nerve cells of the cerebrum, cerebellum, spinal ganglia and especially of the cells of the anterior horns of the spinal cord. It is probable that if the nerve cells were examined in every case of carcinoma, whether the nervous structures were macroscopically involved or not, degenerative changes would often be found.

In almost all of our cases the nerve cells were more or less diseased, and curiously enough, were much more degenerated in the so-called toxic cases than in those in which the nervous structures were the seat of cancer. The extent of the involvement varies, but it may be said that the greater the toxemia, the more the cells are diseased. The alteration of the nerve cells is always diffuse, and is never limited to certain parts of the brain and cord. Thus in Cases VI. and IX. in which clinical signs were found, the degeneration of the nerve cells was not limited to the bulbar nuclei, but involved other parts. Again in Case VII. in which the clinical symptoms pointed to an involvement of different cranial nerves or their nuclei, the degeneration was not limited to these nuclei, but involved others, although symptoms of this extensive disease were not manifest. Again, nuclei of nerve cells may be normal although from the symptoms pathologic changes may be expected.

As a rule, the changes occurring in the nerve cells are not very intense and consist in a displacement of the nucleus to the periphery, and a disintegration of the chromophylic elements. The nerve cells, however, may be intensely diseased and swollen and their chromophylic elements entirely disintegrated.

Whenever toxic symptoms occur, some of the cranial nerves are nearly always involved as in the case of Miura[26], Bettelheim[27], and in Case VII. of our series. Of the cranial nerves, those concerned with ocular movements, and the optic nerves, are most frequently involved. Microscopically the alterations consist principally in swelling of the axis cylinders, the myelin sheath not being much altered. At times the cranial nerves which show involvement clinically, may not be altered pathologically, and *vice versa*. In one of our cases, No. VII. quite a large area of swollen axis cylinders was found on either side of the aqueduct of Sylvius. This indicates that the cancer toxin causes degenerative changes not only in the nerve cells but also in the nerve fibers, whether in the cranial nerves or in the brain itself.

The blood vessels may be the seat of intense congestion as in Case VII. in which many of the small blood vessels in the cerebrum, optic thalamus, cerebral peduncles and pons were intensely congested, especially near the oculomotor nuclei. In places a round cell perivascular infiltration was found.

Clinically, the toxemia of carcinoma may produce a variety of conditions. Coma, mental apathy, psychical disturbances, hemiplegia, monoplegia, convulsions either general or Jacksonian in type, bulbar symptoms and involvement of the different cranial nerves have all been recorded. In fact it may be said that the toxic symptoms due to cancer may be as varied as the symptoms found in hysteria or syphilis.

We have already written upon bulbar symptoms occurring in carcinomata, but because of additional cases we will again consider this subject. The first case of this kind was recorded by Bruns[28], the second and third by us (Cases VI. and IX. [17,29], and the last by Warrington[30]. In the case of Bruns nothing was found microscopically, while in our two cases and in the case of Warrington alterations were found in different nerve cells of the bulb, the alterations, however, were not commensurate with the symptoms. In all of these cases the symptoms were purely bulbar, and consisted in atrophy or paralysis of the tongue and palate, difficulty in talking and swallowing, and dribbling of saliva.

In two additional cases which have come under our observation the symptoms appeared directly after operative procedure, in one after an abdominal operation and in the other after removal of a cancer of the glans penis with subsequent sloughing of the part. It seems as if the disturbance of circulation caused by the operation increased the dissemination of the toxic substance. In one case (No. XI.), besides irregular jerkings of the head and limbs, a paresis of one facial nerve and some nausea and vomiting occurred, the patient had difficulty in pronouncing words and stuttered frequently. These symptoms lasted only a short time and improvement occurred rapidly.

In the other case (No. X.), the symptoms consisted in a loss of function in the muscles of articulation, and at times in complete aphonia. The patient tired very easily, especially in the back and head, and when examined three months after his operation, his speech was slow, monotonous but strong, hesitating but not like that of multiple sclerosis. A throat examination did not show any organic changes. There were no other symptoms.

It is rather difficult to explain why these bulbar symptoms should occur except as a result of a general toxemia, when those functions are disturbed first which are most employed.

We have already mentioned that the cranial nerves are frequently involved in cancer toxemia, and that the ocular muscles may be the seat of paralysis. Thus in the case of Miura there was bilateral optic neuritis and paresis of the oculomotor and abducens nerves; in Bettelheim's case, one third and one seventh nerve were paralyzed, while in Case VII. of our series there was complete internal and external ophthalmoplegia of one side besides a facial palsy.

Psychic symptoms are uncommon in the course of carcinoma. Elzholz[31], in 1898, made a résumé of the literature and collected fifteen cases of cancer with psychoses. Of these, in thirteen there was metastasis in the brain, and he concluded that in most cases, psychic symptoms occur only in metastasis. They may, however, be of toxic origin, as in Case XI., in which the patient's mind was cloudy and the meaining of remarks made to her was not understood; and in another case observed by us in which a patient with a carcinoma of the uterus, but with no metastasis to the nervous system, had periods of excitement.

The psychoses are generally of the confusional type, but occasionally the patients are maniacal or the symptoms may be those of general paresis (Elzholz).

Case I. A woman, 52 years of age, had a cancer of the breast removed two years before she came under the observation of Dr. James Tyson and Dr. C. K. Mills, to whom we are indebted for the notes and the material of this case. She did not have recurrence in the breast, but numerous nodules, evidently cancerous, developed in different parts of the integument and in the upper part of the scalp.

Since the operation she had not been well and was treated for "nervous prostration" several times. She had dizziness, nausea, and irregular headaches, especially in the left orbit and temple. Her vision gradually became impaired, and the limbs weak. The patellar reflexes were exaggerated.

The eyes were examined by Dr. G. E. de Schweinitz, who reported as follows: "Vision, O. D., 3-30; O. S., 3-60. Pupils: right 2. mm., left, 3. mm. Wernicke's reaction sign present. There is palsy of the left levator and left superior rectus muscles. The ophthalmoscope shows the eye grounds to be gray, slightly blurred discs, but no neuritis nor atrophy in any advanced stage. Bitemporal hemianopsia, as shown below, was present." Dr. de Schweinitz thought that from the ophthalmoscopic standpoint a lesion so situated as to involve the posterior part of the optic chiasm and the superior division of the left oculomotor nerve would explain the symptoms.

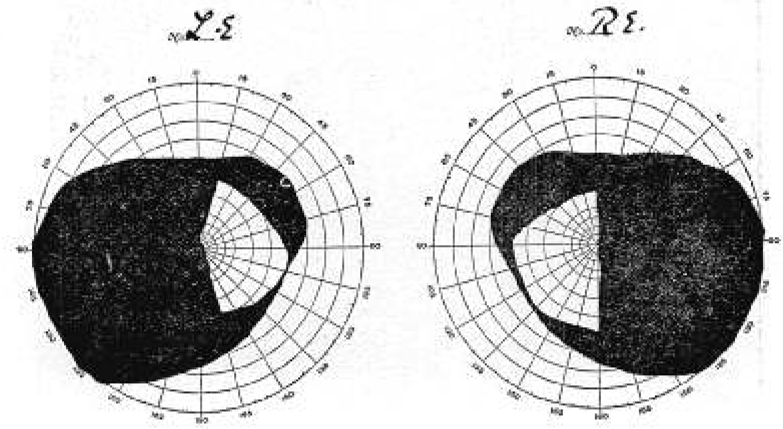

Fig. 1.—Bitemporal Hemianopsia.

The necropsy was performed by us. The examination showed a lump of stony hardness in the exact center of the vertex. On removing the scalp the growth was found to measure one inch laterally and one and one half inches anteroposteriorly. It extended through the calvarium and was adherent to the dura.

The cerebrospinal fluid was not increased in amount, and the brain was not especially edematous. The dura was not adherent to the brain even at the seat of the growth described above.

The sella turcica was much enlarged, being almost one and one half inches in width from side to side, and one inch from before backward. A large tumor mass filled the sella turcica and extended around the optic chiasm and grew into it. It was more extensive on the left side than on the right, and extended as far posteriorly as the anterior part of the pons. The right optic nerve was free from all tumor tissue, the left was attached to the tumor mass.

Scattered throughout the general integument were several hard masses ranging in size from a large hen's egg to a pigeon's egg. The largest of these was within the right scapula. Several smaller nodules were found in the mid-axillary line about the junction of the eighth rib, one in the left groin, and one in the left shoulder. A large tumor mass was also found invading the summit of the uterus.

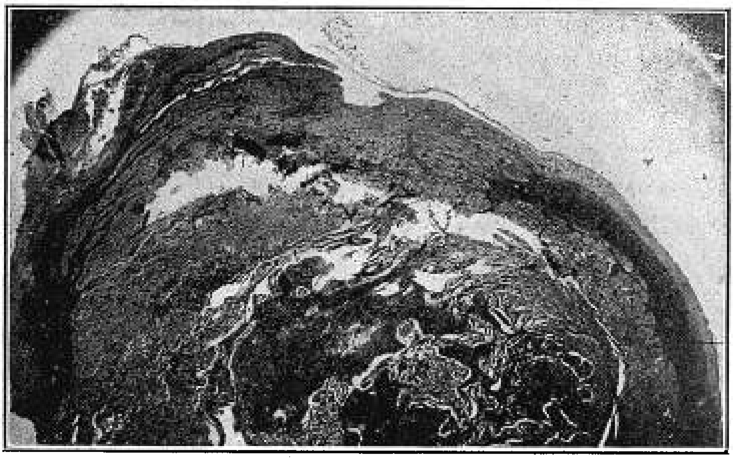

Fig. 2.—Showing Invasion of Chiasm by the Carcinoma; a Few Nerve Fibers of the Chiasm Are Seen on Each Side.

Microscopic examination: The chiasm was much invaded by the carcinoma with great destruction of tissue. The optic nerves did not appear degenerated, or if so, very slightly. A round cell infiltration was found in the pia of the medulla oblongata. A section of the left oculomotor nerve showed invasion by carcinoma cells, and the nerve was adherent to the tumor mass.

Case II. A woman of about sixty, was a patient of Dr. M. B. Dwight, and was seen by one of us with Dr. Dwight and Dr. Wm. Evans. She had had a tumor removed from the right breast twelve years ago, and a few months before she was seen in consultation had had another operation when some tissue, probably carcinomatous, was removed. She was well until eight months before coming under observation, when she complained of pain in the back of the neck, and this region was also tender to pressure.

Examination showed the pupils to be of equal size, the reaction to light was normal. Extraocular movements were normal. There was no involvement of any of the cranial nerves. Sensations for touch and pain were normal over the face.

The patient could not move the right upper limb at the shoulder, but all of the other movements of this limb and of the left upper limb could be performed slowly. Grasp of each hand was feeble, and she had difficulty in picking up a pin. The biceps and triceps tendon reflexes were about normal.

The lower limbs were spastic, and when walking the steps were short, but she did not stagger. The patellar jerks were equally exaggerated, but there was no ankle clonus. The Babinski reflex was uncertain. Sensation was diminished in all four limbs for touch and pain, pain sensation being more diminished in the right upper and left lower limbs. There was no pain on pressure in any of the limbs.

The necropsy was performed by one of us. The carcinomatous mass involved the vertebræ and the surrounding structures from the third to the sixth cervical vertebræ inclusive, rendering the tissues soft. The spinal cord was compressed in this area; the area of softening beginning in the lowest portion of the third cervical segment and involving the fourth, fifth and upper portion of the sixth cervical segments. The carcinoma tissue invaded the dura but did not penetrate it.

Microscopical examination: There was no very distinct degeneration by the Marchi method, either in the cervical or thoracic regions of the cord, although a few black dots were found in the crossed pyramidal tracts. These black dots were not very numerous but could be regarded as a slight secondary degeneration. No degeneration was evident either in the cervical or lumbar regions by the Weigert hematoxylin, or the acid fuchsin hemalum stains. With the thionin stain, some of the cells of the anterior horns were diseased but the alterations were not very distinct. The paralysis in greater part must have been due to a compression of the cord, which was not sufficient to cause intense secondary degeneration.

In the medulla oblongata the Marchi stain showed intense degeneration of the columns of Burdach on each side. The Weigert hematoxylin and acid fuchsin hemalum stains did not show any pathological changes. The cells of the nucleus ambiguus and of the twelfth nucleus were normal.

The Betz cells of each paracentral lobule showed some alteration, the cell body being swollen and the nucleus displaced; there was also considerable disintegration of the chromophylic elements.

A piece of muscle from one hand did not show any degeneration but a piece of nerve showed slight degeneration by the Weigert hematoxylin method.

This case was clearly one of vertebral carcinomatosis, but clinically the intense pains which usually accompany this disease were absent. The pathological findings were not exceptional except that the nerve cells of the anterior horns in the spinal cord and especially the Betz cells of the paracentral lobules were degenerated. This probably was caused by the cancer toxin, as was also the degeneration found in a peripheral nerve, of which no clinical signs had been manifest.

Case III. W. McF., was admitted to the nervous wards of the Philadelphia General Hospital, December 8, 1903. This patient was a man of sixty years and had alcoholic multiple neuritis of the ataxic form, and had in addition the psychosis frequently seen in this disease. He recovered after a long illness and about a year later the only remaining symptoms were those of lost tendon reflexes, slight steppage gait and perhaps a little tenderness on pressure over the nerve trunks of both feet. His mentality at this time was normal.

About one year after the subsidence of the symptoms of multiple neuritis he began to complain of difficulty in swallowing and regurgitated food. Gradually these symptoms increased, until he was unable to swallow anything but liquids. His strength failed, and he became cachectic. An esophageal cancer was diagnosed. Coincident with the appearance of these symptoms he began to complain of pains in his limbs and of great tenderness on pressure over his nerve trunks. These neuritic symptoms gradually grew worse, and became almost as severe as in the previous attack.

He died January 30, 1906. An esophageal cancer was found.

Microscopically, the spinal cord was normal. The nerve cells of the anterior horns were in fair condition. A piece of nerve of one hand showed very intense chronic degeneration, the nerve fibers had almost entirely disappeared. A piece of muscle from the same hand showed considerable atrophy of some of the muscle fibers, with overgrowth of the connective tissue. A piece of nerve teased in the fresh state and stained by osmic acid showed no recent degeneration.

This case illustrates the effect of carcinoma toxin upon peripheral nerves, as shown by the reappearance of the neuritic symptoms.

Case IV. Admitted to the Philadelphia General Hospital, March 13, 1906. The patient was a woman of about 40 years of age who, one year before she came under our observation had a cancer of the left breast removed. About ten months after this she began to complain of radiating pains across the chest and back, and in her lower limbs. A month after this she suddenly lost power in her lower limbs, since which time she has been in bed. She complained of girdle sense but not of extreme pain. Examination showed the cranial nerves to be normal. Her mentality was good. The upper limbs were not involved. She was unable to move her lower limbs and these were in flexor contracture, the legs on the thighs and the thighs on the abdomen. The patellar and Achilles jerks were not obtained on either side. The Babinski response was positive on both sides. Sensations for touch and pain were lost over the lower limbs, abdomen and chest to a point about three inches above the umbilicus, except on the dorsum of each foot, where occasionally a pin prick was recognized. There was incontinence of urine and feces. The diagnosis of vertebral carcinoma was made. The patient died, April 3, 1906. The necropsy showed a carcinomatous involvement of the thoracic vertebræ with a compression of the upper thoracic chord.

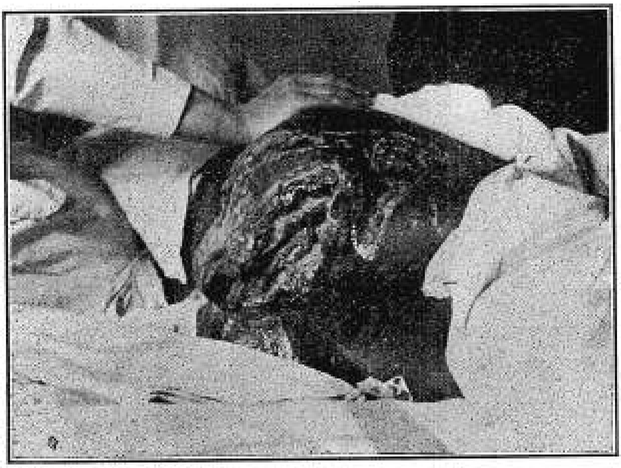

Fig. 3.—Intense Bedsore Occurring with Vertebral Carcinoma.

Case V. Beard, was admitted to the nervous wards of the Philadelphia General Hospital, December 24, 1904. He denied venereal disease. The history obtained was very unsatisfactory. The face and upper limbs were not affected, but the lower limbs were almost completely paralyzed, although some movement was possible at each hip and each knee, and the toes were moved slightly. The patellar reflex was exaggerated on each side, but ankle clonus was not obtainable. Babinski's reflex was distinctly present on each side. Sensations for touch and pain were preserved in the lower limbs, but tactile sensation was diminished on the soles of the feet. Retention of urine was present.

Dr. Knipe reported, January 10, 1906, that the patient had paresis of the left external rectus and of both superior recti, nystagnoid movements on extreme right lateral deviation, severe grade of optic neuritis (partially choked disc) in the right eye, with atrophied spots above following old hemorrhage, and a few fresh hemorrhages near the disc to the inner side. The disc of the left eye was markedly swollen, but not so much as that of the right eye.

There is only one record of any pain in the lower limbs and this was made July 10, 1905.

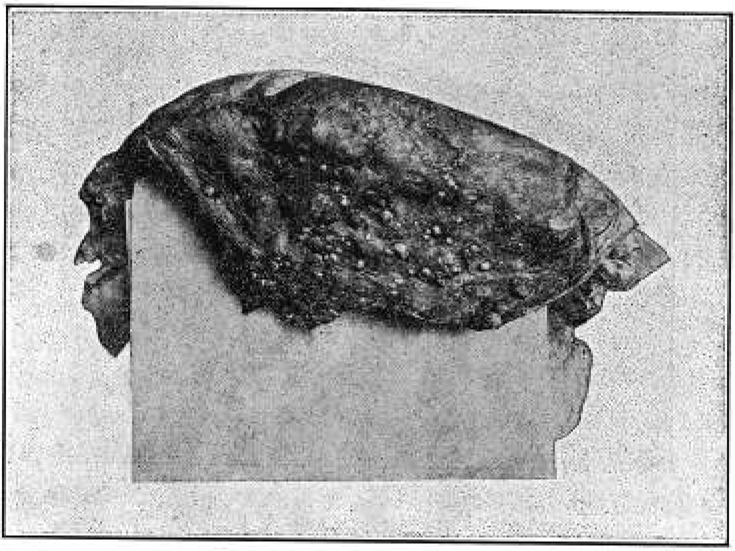

Fig. 4.—Numerous Carcinoma Nodules from the Size of a Millet Seed to that of a Pea on the Inner Surface of the Cerebral Dura.

He came again into the service of one of us in January, 1906. At that time his condition was as follows: He lay in bed with the thighs strongly flexed on the abdomen and the legs flexed on the thighs. He had slight voluntary power in flexion of each thigh, but it was very doubtful whether he had any voluntary movement of his toes. The slight upward movement of the toes which sometimes occurred was probably reflex. The lower limbs were much wasted. The patellar reflex and Achilles tendon reflex were absent on each side. The Babinski reflex was very typical on each side. Tactile and pain sensations were entirely lost in the lower limbs. He had no control of the urine or feces, and the bowels did not move without enema. He moved the upper limbs freely but the movements were weak. These limbs were also wasted. Biceps and triceps tendon reflexes were present on each side, and about normal, considering emaciation which was general. The pupils were equal. The movements of the eyeballs were probably good, though it was impossible to get him to respond promptly. No impairment of cranial nerves was detected. The abdominal muscles were intensely rigid and the abdomen was distended. A necropsy was obtained.

The bone on the whole left side and upper portion of the skull was thickened, and measured about ¾-inch in thickness at the mid portion. The thickening seemed to be caused by the infiltration of a tumor connected with the dura and covering internally the thickened portion of the skull. The tumor (carcinoma) invaded the posterior portion of the second, third and fourth left temporal convolutions; its upper margin began at the lower portion of the second temporal convolution and the anterior margin at the mid portion of the affected convolutions. It involved the tentorium posteriorly. The dura covering the left cerebral hemisphere was thickened and numerous nodules from the size of a millet seed to a pea were found on the inner side of the thickened dura. These were shown to be carcinomata. The spinal dura was adherent at the sixth, seventh and eight thoracic vertebræ, and the bodies of these vertebræ were soft. Carcinomata were found in the liver, ribs and prostate gland.

The absence of all cerebral symptoms, except ocular, in this case was remarkable.

Case VI. This case has been previously reported by us, and only an abstract is given. M. R., a woman, forty-eight years old. Eight years before coming under observation had an abscess(?) of the right breast which ruptured and discharged pus. Four years afterward she began to have sharp shooting pains in her back and around her waist, and later pain in her limbs. Since three weeks after the beginning of her pains she had been confined to her bed. There was extreme atrophy in all of her limbs, more marked in the lower. The upper limbs could be but weakly moved voluntarily. No voluntary movement was possible in the lower limbs. The arm reflexes were present and exaggerated but the reflexes of the lower limbs were absent, probably on account of the extreme atrophy. Sensation was irregularly diminished. She had sharp, spontaneous pains in all of her limbs, and the slightest touch would cause extreme pain. The lower limbs were contracted in flexion. There was a bilateral atrophy of the tongue with fibrillary tremors and weakness in movement.

At the autopsy, metastatic carcinomatous growths were found in the cervical region implicating the bodies of the vertebræ and the surrounding structures, and in two places the growths had implicated the spinal canal. These growths were on the outer surface of the dura and did not penetrate the membrane. The spinal cord was compressed.

In the miscroscopic examination, the carcinomatous masses found outside of the dura, did not penetrate very far into the dura, and distinct carcinomatous tissue was not seen within this membrane. The carcinomatous masses were chiefly on the posterior part of the dura. The spinal cord showed the usual changes of compression myelitis.

In this case we have the typical symptoms of a vertebral carcinomatosis. The bulbar symptoms were unusual.

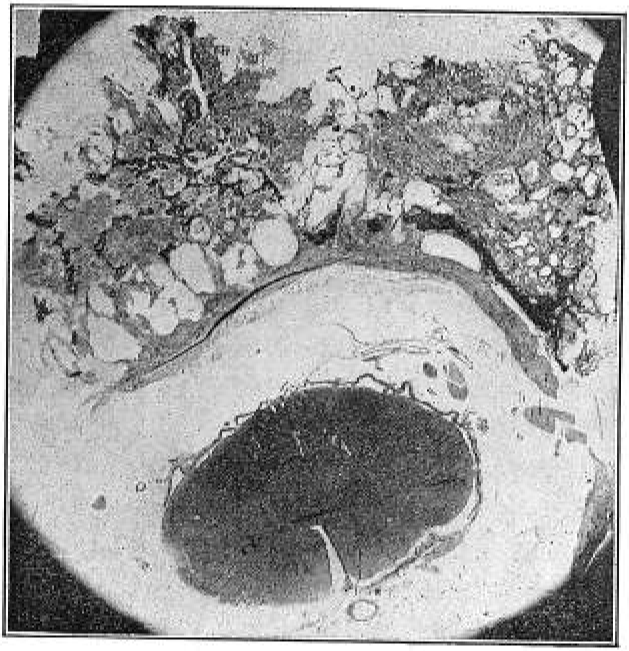

Fig. 5.—Carcinoma on the Posterior Part of the Spinal Dura Not Penetrating the Dura.

Case VII. Was admitted to the Philadelphia General Hospital, September 8, 1903, in the service of Dr. H. B. Allyn, but was transferred to the service of Dr. C. H. Frazier because of fracture of the humerus. The fracture occurred while she was being lifted in bed to an upright position. The notes then made were as follows: "The patient is fifty years of age. A carcinoma of the breast was removed sixteen months before she came under observation, and she has a recurrence in the same place. She complains of pain in the back of the neck and in the hips, especially the left, at the site of operation, and in the back. Five weeks before her admission to the hospital, coincident with the pain in the neck she began to have failure of vision. For several months she has had morning vomiting, and about a year ago she had a swelling at the carpo-metacarpal joint of the left thumb.

There is some exophthalmos of the right eye, but no ptosis. The right pupil is smaller than the left, and responds to light and in accommodation. The right external rectus is paralyzed. She says she can see better with the left eye.

There is ptosis of the left eyelid. The left pupil is larger than normal and does not react to light or in accommodation. The left pupil does not respond to pain stimulus, whereas the right pupil does. Paralysis of the left external rectus and partial paralysis of the left superior rectus exist.

There is no paralysis of the other cranial nerves, nor involvement of the special senses other than that of sight. Both hips are tender and she cannot stand without support."

Other notes made later by one of us (Dr. Spiller) were as follows: "The patient has almost complete ophthalmoplegia, internal and external, of the left eye, and distinct but not equal weakness of the left seventh nerve. She complains of headache over the frontal region, and has had dizziness and weakness of the legs. The patellar reflex is lost on each side, and there is no ankle clonus or Babinski response on either side. She has marked tenderness over the spinal column between the shoulders but no deformity of the spinal column or tumor formation." She died three weeks after her admission to the hospital.

Macroscopical examination did not show any gross changes. The microscopical examination was as follows:

Cranial nerves.—The optic nerves were perfectly normal, both by the acid fuchsin and Weigert hematoxylin stains. A cross section of the optic chiasm did not show any pathological changes.

Some of the axis cylinders of the oculomotor nerves of each side were distinctly swollen.

The left fourth nerve was normal, but some of the axis cylinders of the right fourth nerve were distinctly swollen, but not so much so as those of the third nerve.

The right sixth nerve showed intensely swollen axis cylinders by the hemalum acid fuchsin stain. The left sixth nerve was not obtained.

Some of the axis cylinders of both seventh nerves were swollen, but not nearly so much as those of the right sixth.

Medulla Oblongata.—Sections from the medulla oblongata seemed to be normal. The blood vessels were not congested.

Pons.—The blood vessels within the pons were much congested, and this congestion was more distinct in the posterior part of the pons. There was also some perivascular round cell infiltration. Quite a large area of swollen axis cylinders was found on each side of the aqueduct of Sylvius.

Cerebral Peduncles.—A similar state of congestion was found in the posterior part of the cerebral peduncles, especially around the nuclei of the oculomotor nerves.

Optic Thalamus.—Sections from this area showed intense congestion, there was also a slight perivascular infiltration around the blood vessels.

Cortex.—There was considerable congestion in sections from each frontal and each occipital lobe, but not nearly so much as in the pons and cerebral peduncles. The cerebellum was normal.

Nerve Cells.—Many of the cells of the third nerve on each side were distinctly diseased, being swollen, presenting chromophylic changes involving all parts of the cell, and the nuclei were displaced to the periphery. Many of the cells of these nuclei were normal.

The sixth nucleus on each side was very much affected, if anything more so than the oculomotor, and in a similar manner.

The seventh as well as the twelfth nucleus on each side was perfectly normal. The nucleus ambiguus of one side, the Betz cells of each paracentral lobe, and the nerve cells of each occipital and frontal lobe were in a healthy condition, but some of the cells of Purkinje showed some displacement of the nucleus.

The symptoms in this case were probably caused by the carcinoma toxin. This case illustrates well the widespread effect of such a condition, and the pathological changes found in the nerve cells, blood vessels and cranial nerves are typical.

Case VIII.—A woman about 60 years of age, was seen in consultation by one of us with Drs. L. W. Steinbach and Dr. David Riesman. Two years before this examination a carcinoma of the left breast was removed by Dr. Steinbach, and for the past fifteen months she has had pain and swelling in the left knee, and pain in the neck for about seven weeks.

There was no cachexia and intellect was clear. Vision in the right eye was good, in the left eye a cataract operation had been performed. The light reaction in the right eye was prompt, all the cranial nerves were normal.

The movements of the neck were restricted in all directions. She could move her head from side to side and backwards and forwards slightly, but the movements caused pain. Turning her in bed caused excruciating pain. There was a swelling in the spinal column in the back of the neck.

It was impossible for her to move the left upper limb at the shoulder, but she could flex the left forearm on the arm freely. The grasp of each hand was normal. Movement in the right upper limb was good. The biceps and triceps tendon reflexes were exaggerated on both sides, much more so on the right side. Sensations for pain and touch were normal everywhere.

Much numbness and pain were present in the left upper limb.

There was no voluntary movement in either lower limb, except in the toes where movement was free. The left thigh seemed smaller than the right. The patellar reflexes were exaggerated, more so on the left, as shown by the prompter contraction of the quadriceps, rather than by movements of the leg. The Achilles jerk was not distinct on either side, and the Babinski response was not obtained, the toes not moving on plantar irritation. Any movement of the lower limbs caused intense pain. There was no tenderness to pressure over the spinal column.

This patient also showed the usual symptoms of vertebral carcinomatosis. She subsequently died, but an autopsy was not permitted.

Case IX.—This case has been reported by one of us in a previous communication and only a short abstract will be given. A woman of fifty-nine years developed a cancer of the right breast thirteen years previously. Five months before her death she began to complain of difficulty in swallowing and talking. When examined a month before her death she could talk only in a whisper and could swallow fluids only with difficulty. There was no atrophy of the tongue, lips or face.

At the autopsy no macroscopic lesions were found, but microscopic examination showed an alteration in some of the nerve cells of the nuclei of the sixth, seventh, ninth and tenth cranial nerves.

This was the third case of bulbar symptoms occurring in carcinoma reported, and the first in which bulbar symptoms occurred alone. These were not due to an alteration of some of the nerve cells, but to the general intoxication.

Case X.—A man of forty-one years, with an excellent family and past history, was sent to one of us for opinion by Dr. W. M. Robertson, of Warren, Pa., with the following history: Three months before he came to Philadelphia he was seen by Dr. Robertson, the patient then having a cancer of the glans penis, following phimosis. A few days later the part was amputated and the inguinal glands removed. Several days after this he developed a cystitis and urethritis from the retention catheter, and at the same time the end of the stump sloughed. These symptoms caused a high temperature for a few days.

The condition of the patient was good during the fever, but when it left, there was loss of function of the muscles of articulation and at times complete aphonia. The mental condition was good. He also had some photophobia and double vision. After a week his voice returned somewhat but did not fully recover its former quality. Examination by one of us three months after the onset of the cancer symptoms showed the pupils to be normal in size, the reaction to light, accommodation and convergence normal. Extraocular movements were not impaired. The facial and trigeminal nerves were normal on either side. Sensations for touch and pain were normal over the face.

The upper limbs were not weak, but there was not much resisting power. There were no subjective pains. Sensations for touch, pain and temperature were normal in the forearms and hands. The biceps and triceps tendon reflexes were normal. Power in the lower limbs was normal. The patellar and Achilles jerks were normal. The Babinski sign was not obtained. Sensations for touch, pain and temperature were normal over the feet.

The voice was slow, monotonous but strong; hesitating but not like that of multiple sclerosis. The patient would tire easily, especially in the back of the head and neck. After an automobile ride he became extremely exhausted and had complete aphonia. Weakness was so great that he could not turn in bed. All voluntary muscles moved slowly.

Dr. Freeman examined the throat and reported that there was no organic disease of this part. There was some congestion of the larynx and trachea which made speaking a little difficult and caused the patient to clear his throat, but Dr. Freeman did not believe that this had any influence on his curious manner of speaking. The tissues of the larynx were relaxed and there was a marked sluggishness in the action of the laryngeal muscles. Dr. Freeman considered the difficulty in speaking as caused by mental disturbance and believed that time would bring about a full recovery.

In this patient the weakness of the muscles of articulation may have been caused by the cancer toxin, and was really part of the general weakness with which the patient suffered. It is a striking fact that these symptoms did not come on until after the removal of the growth and the appearance of sloughing of the part. This can probably be explained as in the following case, by the dissemination of the toxin by the circulation. Some of the features suggest myasthenia gravis.

A letter received from Dr. Robertson, February 12, 1906, is as follows: "Mr. E.—— has done quite well. His improvement is slow but constant. He has grown fleshy. I have been a little in doubt as to whether or not there is present a certain caste of mind like that of senility. The speech is not right, but is better than when you saw him. I can see no evidence of the original trouble being present."

Case XI.—Was seen by one of us in consultation with Dr. Marie Formad. A short time before the examination a carcinoma of the uterus and ovaries had been removed by Dr. Formad. Numerous minute carcinomatous nodules were found in the peritoneum and could not be removed.

A short time after the operation she began to have constant headache, either in the right or left side of the forehead. She also vomited considerably and had occasionally dizziness.

When examined she understood all that was said to her, but at times her mind seemed a little cloudy and she did not grasp immediately the meaning of a remark made to her. She was not aphasic, although at times she had difficulty in pronouncing the word she wished to say and frequently stuttered. Her enunciation was distinct. She could count fingers correctly with each eye, but she acted as though her vision were not entirely normal.

The pupils were equal and the iritic response to light prompt in each eye. Extra-ocular muscles were normal. There was no hemianopsia. There was a slight weakness in the distribution of the right facial nerve as shown by the incomplete elevation of the brow and of the corner of the mouth on that side. The masseter contracted well on each side and hearing was good. There was no rigidity of the neck and movements of the head were free.

The upper limbs were well developed and power was about normal. The biceps and triceps tendon reflexes were prompt on each side, probably a little prompter on the right side. The tonicity of the muscles was about normal.

The lower limbs were distinctly weak. The patient could perform all movements, but had little power if any resistance was offered. The tonicity of the muscles was about normal. The patellar reflex was exaggerated on each side, and there was a tendency to patellar clonus on each side; but the clonic movements were abortive and soon ceased. The Babinski reflex could not be obtained because the patient was very ticklish on the soles of the feet. There was no atrophy of the limbs.

Sensations for touch and pain were normal all over the body. Constant involuntary jerkings of each side of the face were present during the examination, jerkings were present also in both the upper and the lower limbs, but not so constantly as in the face. Gait and station could not be tested because the operation had been too recent. The patient improved considerably under treatment.

The symptoms in this case appeared after the operation, and it is probable that the disturbance of circulation caused by the operation increased the dissemination of the toxic substance from the numerous carcinomatous masses remaining in the peritoneum.

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